

CLAIMS

1. A therapeutic composition comprising a regulatable agent and an agent that binds to a cell surface element of a mononuclear phagocyte.
2. A therapeutic composition according to Claim 1 wherein said regulatable agent is a hypoxia and/or ischaemia and/or stress regulatable agent.
3. A therapeutic composition according to any preceding Claim wherein said regulatable agent comprises a therapeutic gene.
4. A therapeutic composition according to Claim 3 wherein said gene is under the control of a hypoxia and/or ischaemic and/or stress sensitive agent.
5. A therapeutic composition according to any preceding Claim wherein said binding agent comprises a ligand adapted to bind to said cell surface element.
6. A therapeutic composition according to any preceding Claim wherein said binding agent comprises means for ensuring said regulatable agent is internalised into said mononuclear phagocyte.
7. A therapeutic composition according to Claim 6 wherein said means further is adapted to ensure that said therapeutic gene is incorporated into the nucleus of said mononuclear phagocyte.

8. A therapeutic composition according to ~~Claims 1-7~~ wherein said binding agent is a viral vector.
9. A therapeutic composition according to Claim 8 wherein said vector is an adenoviral vector.
- 5 10. A therapeutic composition according to Claim 8 wherein said vector is a retroviral vector.
11. A therapeutic composition according to ~~Claims 1-6~~ wherein said binding agent includes mannosylated poly-L lysine.
12. A therapeutic composition according to ~~Claims 3 to 11~~ wherein said gene encodes a pro-drug activation enzyme.
13. A therapeutic composition according to ~~any preceding Claim~~ wherein said regulatable agent further, or alternatively, comprises a bioreductively activated pro-drug.
14. A therapeutic composition according to ~~any preceding Claim~~ wherein said composition further comprises an agent that activates or controls said regulatable agent.
15. A therapeutic composition according to Claim 14 wherein said agent controls the expression of a gene encoding an activating or control product.

therapeutic gene is under the control of an inducible or repressible promoter element.

17. A therapeutic composition according to Claim 16 wherein said element comprises a selected repressor DNA sequence.

18. A therapeutic composition according to Claims 3 or 17 wherein there is further provided a gene encoding a protein that kills mononuclear phagocytes.

19. A mononuclear phagocyte that has coupled thereto, or internalised therein, at least a hypoxia and/or ischaemia and/or stress regulatable agent and, optionally, an agent that is adapted to bind to a mononuclear phagocyte ligand which is typically found on the cell surface of said mononuclear phagocyte.

20. A method for selectively destroying a mononuclear phagocyte comprising attaching thereto, or internalising therein, a cytotoxic, hypoxically and/or ischaemically and/or stress activated agent; and exposing said mononuclear phagocyte to hypoxic and/or ischaemic and/or stress conditions that occur either artificially by induction or occur/exist naturally.

21. A delivery system for targeting therapeutic compositions to hypoxic and/or ischaemic and/or stress sites comprising a hypoxia and/or ischaemia and/or stress regulatable agent and an agent for controlling the functional effectiveness thereof, and coupled thereto, a binding agent for a cell surface molecule of a mononuclear phagocyte.

22. A method for targeting desired agents to hypoxic and/or ischaemic and/or stress sites comprising:

- 5 i) coupling at least one of said agents to a binding agent that is adapted for binding or targeting a cell surface molecule expressed by a mononuclear phagocyte;
- ii) exposing said coupled agent to a mononuclear phagocyte; and allowing said mononuclear phagocyte to migrate, under conditions that support migration, either on *in vitro* or *in vivo*.

10 23. A method for treating conditions associated with hypoxic and/or ischaemic and/or stress states comprising administering to an individual to be treated a therapeutic composition according to ~~Claims 1-18~~.

15 24. A method for treating conditions associated with hypoxic and/or ischaemic and/or stress states comprising; withdrawing blood and/or serum from an individual to be treated and treating said blood and/or serum *in vitro* with a hypoxically and/or ischaemically and/or stress inducible therapeutic gene under conditions that enable incorporation of said gene into the nucleus of mononuclear phagocytes and re-injecting said treated blood and/or serum into the individual either systemically or directly into a hypoxic and/or ischaemic and/or stress area.

1 1 1
1 1 1